A Report On
African Animal Trypanosomiasis
presented to

The United States Agency for International Development

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July, 1980
AFRICAN ANIMAL TRYPANOSOMIASIS
A Study of Research and Research Needs

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Preface

This study of African Animal Trypanosomiasis was made under the auspices of the United States Agency for International Development (USAID). It was prompted by the USAID's continued interest in studying animal disease that present a serious threat and impediment to food production and human welfare in the lesser developed countries of the world.

The major objectives of the study were to provide:

1. background material as to the nature of the disease and the problems that it poses to the lesser developed countries of the world;
2. conclusions and recommendations for research;
3. a bibliography of published material;
4. abstracts of recently published research information;
5. a description of the nature of research currently being conducted; and,
6. supplementary materials recommended for reading.

These objectives were used as a format to provide a comprehensive document consisting of four volumes. The document is intended to be used as a means of informing expeditiously USAID officials and advisory committees on the subject.

The study was conducted by searching the literature and personally visiting with many of the world's experts on the subject. Literature citations from 1900 to 1980 have been made. Abstracts of most of the literature published from 1973 to 1980 are provided.

Personal discussions were held on the subject of African Animal Trypanosomiasis with scientists of the USDA-Laboratory on Insects Affecting Man and Animals; the Walter Reed Medical Institute; the Tsetse Research Laboratory University of Bristol School of Veterinary Science; the Ministry of Overseas Development, United Kingdom; the Food and Agriculture Organization; the International Atomic Energy Agency of the
United Nations; the Institute d'Elevage et de Medicine Veterinaire des Pay Tropicaux; the International Livestock Center for Africa; the International Center of Insect Physiology and Ecology; the Inter-African Bureau of Animal Resources; the International Laboratory for Research on Animal Diseases; the Ministry of Agriculture of Kenya; the Onderstepoort Veterinary Research Institute of South Africa; and the Rockefeller Foundation.

The technical capabilities and generosities of the scientists contacted in national and international agencies, private industries, foundations, and state, national and international laboratories, are acknowledged. The excellent reports of the U.S. Department of Agriculture, the Food and Agriculture Organization and The World Health Organization of the United Nations were rich sources of information.

The author wishes to thank all contributors for their assistance in providing information for this study. Appreciation is especially given to Dr. C. John Mare, who with first-hand knowledge of the disease, assisted in preparing the portion of this report dealing with the nature of the disease.

The study of this disease and the threat that it poses to the food production, human health and economic welfare of the lesser developed countries of Africa has impressed on me the need for USAID to develop a research support program in order to control the disease.
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Volume I

A. THE DISEASE AND THE PROBLEM
NATURE OF THE DISEASE

Introduction: The protozoan parasites of the genus *Trypanosoma* are without doubt the single most important group of disease-producing agents in the 5 million square miles of Africa south of the Sahara desert. These parasites affect millions of people, both by their disease-producing capacity in humans, and by their devastating effects on man's domestic animals. The enormous loss of the four great "M's" of Africa, namely meat, milk, manure and motive power, results in widespread misery in the trypanosome-infested areas of Africa.

The pathogenic trypanosomes of Africa include *Trypanosoma congolense*, *T. vivax*, the trypanosomes of the *T. brucei* subgroup (*T. brucei brucei*, *T. brucei gambiense* and *T. brucei rhodesiense*), *T. simiae*, *T. evansi* and *T. equiperdum*. Only the first three of the eight above-mentioned trypanosomes are considered to be the causes of "Nagana" or "tsetse fly disease" in animals, and these trypanosomes will form the basis for this discussion. *Trypanosoma brucei gambiense* and *T. b. rhodesiense* are the causes of human sleeping sickness, a severely debilitating, often fatal disease, occurring in West, Central and East Africa. In West and Central Africa, a chronic form of human sleeping sickness is caused by *T. b. gambiense*, a trypanosome which has man as its major host, but which does infect pigs. In East and Southern Africa, *T. b. rhodesiense* is the cause of a much more acute form of human sleeping sickness. This trypanosome also infects cattle, bushbuck (*Tragelaphus scriptus*) \(^{21}\), and probably many other wild animals \(^{19,39,47}\) which may serve as reservoirs of the parasite.
Trypanosoma simiae causes acute disease in pigs and camels, and subclinical infection in warthogs (Phacocoerus aethiopicus) which serve as reservoirs of T. simiae. This parasite is mechanically transmitted by biting flies other than tsetse flies (Glossina spp.), but can be transmitted cyclically by the tsetse fly.

Trypanosoma equiperdum is the cause of dourine, a venereally transmitted disease of horses, and T. evansi is the cause of surra, a North African and Asian disease of camels, horses and dogs.

"African animal trypanosomiasis", widely known as "nagana", is a collective term comprising infection with T. congolense, T. vivax and T. brucei brucei. The disease is most important in cattle, but it can cause serious losses in pigs, camels, goats and sheep. The trypanosomes are biologically transmitted by tsetse flies (Glossina spp), and mechanical transmission by other biting flies (especially with T. vivax) can be the major mode of transmission.

Infection of cattle with the three nagana trypanosomes results in subacute, acute or chronic disease characterized by intermittent fever, anemia, diarrhea and rapid loss of condition, often terminating in death. The name "nagana" is derived from the Zulu language, and means "to be in low or depressed spirits", a very apt description of the clinical disease. The name "tsetse" is derived from the Sechuana and means "cattle-destroying fly".

History and Distribution: The Boer settlers in South Africa left accounts of the ravages of the tsetse fly, and David Livingstone, the intrepid Scottish missionary explorer described the disease and incriminated the tsetse fly in 1857. In his "Popular Account of Missionary Travels and Researches in South Africa" he describes the fly and the effect of its bite as follows: "Its bite is death to the ox, horse and dog. In this journey, though we watched the animals carefully and believe that not a score of flies were ever upon them, they destroyed forty-three fine oxen".
In 1894 Sir David Bruce showed that trypanosomes were the cause of the disease, and it was he who first publicized the name "nagana".

The disease remained widespread throughout East and Southern Africa, where it was first recognized, until the major rinderpest pandemic of 1890-1898 decimated the domestic and wild ruminant populations. This massive destruction of antelope, the reservoir hosts of the trypanosomes and the main source of feed for the principal vector in the area, *Glossina pallidipes*, resulted in marked reduction in the size of the affected areas, and only with the advent of game preservation laws did the wild ruminants, and consequently nagana, once again become widely established. Nearly two-thirds of tropical and sub-tropical Africa (an area of nearly 5 million square miles) is infested with the tsetse fly. As may be seen from Figure 1, this area extends from the southern edge of the Sahara desert in the north (15° N latitude) to Angola, Zimbabwe and Mozambique in the south (20° S latitude). Much of this vast area is rendered unsuitable for intensive human habitation, and especially for livestock production as may be seen from Figure 2. Nagana seems to be spreading in parts of Africa where tsetse control methods have been abandoned, but in some countries, where these methods are applied the disease remains confined. Nagana was eradicated from South Africa in 1962.

**Etiology:** The three animal trypanosomes around which this discussion revolves belong in the salivarian section of the genus *Trypanosoma* in the family *Trypanosomatidae* of the order *Protomonadida*.

*Trypanosoma congolense* resides in the subgenus *Nannomonas*, a group of small trypanosomes with medium-sized marginal kinetoplasts, no free flagellum, and weakly developed undulating membranes. *Trypanosoma congolense* is a
Figure 1
DISTRIBUTION OF THE TSE-TSE FLY

[Map of Africa showing the distribution of the Tse-Tse fly with various countries and cities labeled.]
small monomorphic member of this subgenus, and in East Africa is considered to be the single most important cause of nagana, especially of cattle. This trypanosome is also a major cause of the disease in West Africa. Cattle, sheep, goats, horses and pigs may suffer serious disease with T. congolense infection, and in domestic dogs chronic infection resulting in a carrier state is often seen.

Trypanosoma vivax resides in the subgenus Duttonella, a group of trypanosomes with large terminal kinetoplasts, distinct free flagella and inconspicuous undulating membranes. Trypanosoma vivax is a large (18-26mm long), monomorphie organism, very active in wet-mount blood smears. Cattle, sheep, and goats are primarily affected, and while this organism is considered to be less virulent for cattle than T. congolense, it is nonetheless the most important cause of nagana in West African cattle. Dogs may undergo chronic infection and remain carriers. This trypanosome readily persists in areas free of tsetse flies, for example, in Central and South America and the Caribbean where it is transmitted mechanically by biting flies. Trypanosoma uniforme (also subspecies Duttonella) is similar to T. vivax (considered synonyrne to T. vivax by some), slightly smaller, and causes similar disease.

Trypanosoma brucei brucei resides in the subgenus Trypanozoon, a heterogeneous group of organisms with well-developed broad undulating membranes and small subterminal kinetoplasts. Trypanosoma b. brucei is an extremely polymorphic organism occurring as short, stumpy organisms without flagella, long, slender organisms with distinct flagella, and intermediate forms, usually flagellated. This organism is very closely related to T. b. gambiense and T. b. rhodesiense (see introduction). Horses, dogs, cats, camels and pigs are very susceptible to T. b. brucei infection, but
infection of cattle, sheep and goats, and sometimes pigs often results in mild or chronic disease. This last ob­
servation, while widely accepted, has been called into quest'ion by Moulton and Sollad41 who cite evidence show­
ing that this organism is widespread in East and West Africa, and that it can cause serious disease and high mortality in cattle, sheep and goats.

Animal susceptibility: Cattle, sheep, goats, pigs, horses, camels, dogs, cats and monkeys are susceptible to nagana and may suffer syndromes ranging from subclinical, mild to chronic infection to acute fatal disease. Rats, mice, guinea-pigs and rabbits are useful laboratory species.

More than thirty species of wild animals have been shown to become infected with pathogenic trypanosomes2,5,37, and many of these can remain carriers of the organisms. While one tends to conclude that ruminants are the principal carriers it has been shown that wild equidae37,39, lions3,40,47, leopards3 and wild pigs2 are all susceptible and can serve as carriers of the trypanosomes. It has been widely accepted that wild animals are trypano-tolerant; that they will all resist infection and remain carriers of the parasite43. That this is not true has been demonstrated by Ashcroft et al.2 who showed by needle challenge with T. b. brucei that wild animals fall into three distinct classes of susceptibility. First of all the refractory group (baboons), secondly the relatively resistant animals that do become infected and parasitemic, but show little clinical evidence of disease (warthog, bushpig, porcupine, bushbuck, oribi, common duiker, impala, eland, Bohar reedbuck and spotted hyena), and thirdly, the very susceptible species which sick­
en with the disease and often die (jackal, serval, hyena, monkey, antbear, bat-eared fox, dik-dik, Blue Forest duiker and Thompson's gazelle). It is probable that other species of wildlife, not tested in this study, are susceptible to T. b. brucei, and it is also probable that a range of sus­ceptibility will be demonstrated when wild animals are test­ed for their resistance to T. congolense and T. vivax.
Extensive studies designed to ascertain the susceptibility of wildlife species to the nagana trypanosomes need to be undertaken, and controlled studies should be performed to determine the duration of the carrier state in infected wildlife.

An interesting observation made by Ashcroft et al.\textsuperscript{2} was that tsetse flies preferred feeding on species in the resistant group (especially warthogs) over the highly susceptible species. The warthog is considered one of the prime reservoirs of the nagana trypanosomes.

**Symptoms:** Since simultaneous infections with more than one trypanosome species are not uncommon, and simultaneous infection with trypanosomes and other hemoparasites (Babesia spp., Theileria spp., Anaplasma spp., Erlichia spp.) are extremely common, it has been difficult to conclude which clinical signs are attributable to a given parasite. Few adequately controlled studies have been made, and thus a "typical" clinical response to each trypanosome is difficult to reconstruct. What follows is a summation of the syndromes observed in field and experimental cases of nagana caused by each of the three nagana trypanosomes.

The cardinal clinical sign observed in nagana is anemia\textsuperscript{15,28,38}. Also invariably present are intermittent fever, edema and loss of condition\textsuperscript{22}. The severity of the clinical response is dependent on the species of animal, the species of trypanosome, the nutritional status of the affected animal and the dose and virulence of the infecting trypanosome. Stress plays a prominent role in the disease process, and under experimental conditions, where stress may be markedly reduced, it is often very difficult to elicit clinical disease.

*Trypanosoma congolense* is a hematic trypanosome which is found only in the blood vessels of the animals it infects\textsuperscript{34}. It does not localize and multiply outside blood vessels. Infection with *T. congolense* may result in peracute, acute or chronic disease in cattle, sheep, goats, horses and camels,
with pigs often showing milder disease, and chronic disease being common in dogs. The incubation period may vary from 4 to 24 days, and is followed by intermittent febrile episodes, depression, lethargy, weakness, loss of condition, anemia, salivation, lacrimation and nasal discharge. As the disease progresses, one sees loss of condition and hair color changes from black to metallic brown. The back is often arched and the abdomen tucked up. Accelerated pulse and jugular pulsation occurs and breathing is difficult. Anemia is a prominent sign. The organisms are readily demonstrable in blood smears, especially early in the infection. In the more chronic forms of the disease, enlarged lymph nodes are seen and organisms are most readily demonstrated in lymph node smears.

*Trypanosoma vivax* has a very variable incubation period (5-10 days) and causes severe fatal infection in horses, camels, dogs and cats. It usually causes mild, chronic, or sub-clinical disease in cattle, sheep, goats and pigs. A febrile response occurs in the horse 4-14 days after infection. This is followed by recurrent febrile reactions. The heartbeat and respiration may be accelerated, and loss of condition and weakness is seen while the appetite remains good. Progressive anemia and edema of the ventral regions, especially the male genitalia, are characteristic. The organisms are not always easily demonstrated in blood smears, and since this is a humoral trypanosome, it is best demonstrated in tissue smears or sections, (e.g. lymph nodes). Infected animals die in a few weeks or several months depending on the virulence of the strain of *T. b. brucei*.

**Pathological lesions:** In spite of the rapid advances that have occurred in man's knowledge of African animal trypanosomiasis, there remains a remarkable void in the areas of pathology and pathogenesis of this group of diseases. Recognition of this fact has recently led Losos and his co-workers to carefully explore and document the lesions caused by these parasites. Much needs to be done in this
area, but a good start has been made. One of the problems with early descriptions of the pathology of nagana was a lack of recognition of the fact that mixed infections with hemoparasites frequently occur, thus complicating the pathological syndromes.

The pathogenesis of the disease is now receiving much-needed attention, and recent work by Tizard, Kobayashi and others has contributed greatly to the current understanding of these very complicated diseases. What follows is a summary of the current understanding of the pathology and pathogenesis of nagana.

No pathognomonic changes are seen in nagana. Anemia, edema, and serous atrophy of fat are commonly seen. Subcutaneous edema is particularly prominent and is usually accompanied by ascites, hydropericardium, and hydrothorax. The liver may be enlarged or atrophic, and edema of lymph nodes is often seen. The spleen may be swollen, normal, or atrophic. Necrosis of the kidneys and heart muscle and subserous petechial hemorrhages commonly occur. Gastroenteritis is common, and focal polioencephalomalacia may be seen. A localized lesion (chancre) may be seen at the site of the fly bite, especially in goats. The anemic blood changes are anisocytosis, poikilocytosis, polychromasia, and punctate basophilia. All, some, or none of the above lesions may be seen!

The lesions caused by the trypanosomes in susceptible host species vary considerably depending on the species and strain of trypanosome and the species of host animal affected. In the susceptible bovine, the lesions produced by the hematic trypanosomes, T. congoense and T. vivax, (found mainly in the blood), differ greatly from the lesions produced by T. b. brucei which localizes in the tissues. The hematic trypanosomes cause injury to the host mainly by the production of severe anemia. In the early phases of infection, when blood parasite levels are high, this anemia appears to be directly trypanosome-related, possibly caused
by a trypanosome hemolysin which has been demonstrated\textsuperscript{51}. At the same time increased phagocytic activity results in massive erythrocyte destruction. A combination of parasitemia and anemia results in malfunctioning of the circulatory system resulting in some of the lesions (e.g., ascites, hydropericardium, hydrothorax, edema) described above. In later stages of infection, after the disappearance of the trypanosomes from the peripheral circulation, erythrocyte destruction continues, mainly by erythrophagocytosis\textsuperscript{52}. The stimulus for this late erythrocyte destruction remains obscure.

Within a week after infection with the hematic trypanosomes there is usually a pronounced decrease in PCV, Hb, RBC and WBC levels which may drop to below 50% of pre-infection levels within two months\textsuperscript{34}. The development of anemia and leucopaenia is accompanied by steady loss of weight. In the terminal stages of disease caused by the hematic trypanosomes focal polioencephalomalacia is observed, probably caused by ischemia resulting from the massive accumulation of the parasites in the terminal capillaries of the brain. This parasite accumulation in the microcirculation is also seen in the heart and skeletal muscles\textsuperscript{33,34}.

The lesions produced by the humoral parasite T. b. brucei are remarkably different from those seen with the hematic trypanosomes. Anemia is an important lesion, but much more dramatic are the inflammation, degeneration and necrosis resulting from intercellular invasion of various organs\textsuperscript{33}. Marked proliferative changes reflecting immunological response are observed in the lymph nodes and spleen, and mononuclear cell infiltration and edema are observed in most body tissues\textsuperscript{41}.

Immunological lesions are significant in trypanosomiasis and it has been suggested\textsuperscript{52} that many of the histological lesions observed in these diseases (e.g., anemia, glomerulonephritis) may be the result of the deposition of immune complexes which interfere with, or prevent, normal function. The most significant and complicating factor in the pathogenesis
of trypanosomiasis is the profound immunosuppression which occurs following infection with these parasites\textsuperscript{36,52}. Marked depletion of T-lymphocytes occurs with destruction of lymphoid tissues\textsuperscript{12,33}, serum complement levels are significantly decreased\textsuperscript{30} and serum immunoglobulin levels are severely disrupted\textsuperscript{30,36}. The role of the hemolytic, mitogenic and immunosuppressive fatty acids described by Tizard et al.\textsuperscript{51,52} in the pathogenesis of trypanosomiasis is probably profound and evidence linking these factors with the tissue damage observed is rapidly emerging.

The marked immunosuppression resulting from trypanosome infection lowers the host's resistance to other infections resulting in secondary disease which greatly complicates both the clinical and pathological features of nagana. Diagnosis: The clinical signs and pathological lesions taken together are not characteristic enough to allow definitive diagnosis of nagana. It is necessary to proceed further and demonstrate the presence of the causative parasites.

In the early phases of infection, especially with hematie trypanosomes, the parasites can be readily observed by microscopic examination of wet-mount blood slides. Thick blood films, fixed and stained with Giemsa are also a good technique, but in thin blood films, which are favored for species identification, the parasites may be hard to demonstrate. When parasitemia is low, smears of buffy coat (obtained by microhematocrit centrifugation) can be useful for demonstration of the parasites. Since \textit{T. congolense} tends to associate with the erythrocytes, it is essential that buffy coat and adjacent erythrocytes be included in the smear to ensure demonstration of the parasite\textsuperscript{42}.

Stained lymph node smears are a very good method for diagnosis, especially for \textit{T. vivax} and \textit{T. b. brucei}. In chronic \textit{T. congolense} infection the localization of the parasites in the microcirculation of the lymph nodes may
may allow diagnosis by lymph node smear, but early in infection, blood smears are optimal for demonstration of this parasite.

Both *T. congolense* and *T. b. brucei* readily infect rats and mice which are useful for the detection of these parasites. Intraperitoneal inoculation with blood, spleen and lymph node suspensions readily infect those species, in which the parasites can then be demonstrated. *Trypanosoma congolense* can also be diagnosed by guinea pig inoculation, and *T. b. brucei* by rabbit, dog and cat inoculation. *Trypanosoma vivax* does not readily infect laboratory animals.

An indirect fluorescent antibody procedure using dried blood samples is a useful diagnostic tool, but this technique is not often used since a combination of some or all of the above-mentioned procedures usually results in diagnosis.

**Transmission:** The major biological vectors of nagana in animals and sleeping sickness in man are the flies of the genus *Glossina*, the tsetse flies. There are more than twenty species of the genus, all of them occurring on the African continent, and only one (*G. tachinoides*), occurring elsewhere, namely on the southern Arabian peninsula.

The tsetse flies are dark brown to yellowish flies, varying in length from 6mm (*G. tachinoides*) to 13mm (*G. longipennis*). They all have prominent proboscii, and most have elongated palpi. When at rest the wings are crossed scissor-like, covering the abdomen. The wing venation is very characteristic, with the discal cell shaped like a meat cleaver (referred to as the "cleaver cell").

The tsetse flies occur in "fly belts" determined by proximity to water, adequate tree cover for breeding, hot environment, and sufficient animals to feed on. They have an extremely wide host range, and will feed on mammals, birds and reptiles, but given their choice will select one species over another. 


The tsetse flies can be divided into three main groups; the *G. morsitans* group which favor the open woodland of the savanna country, the *G. palpalis* group, which prefer a shaded habitat immediately adjacent to lakes and rivers, and the *G. fusca* group which favor higher denser forest, and are thus far less prone to come into contact with cattle than the flies of the other two groups. The most important vectors of nagana are found in the *G. morsitans* group which inhabit the best livestock habitat.

The tsetse are slow-breeding flies with larval development taking place *in utero*, one full-grown larva being extruded every 10 to 15 days throughout the life-time of the female fly. Each female produces 8 to 10 larvae during a lifetime, and requires several blood-meals during the development of each larva.

Trypanosomiasis is also mechanically transmitted by tsetse and other biting flies. The most important mechanical vectors are flies of the genus *Tabanus*, but *Haematopota, Liperosia, Stomoxys* and *Chrysops* flies have also been incriminated. In Africa both *T. vivax* and *T. b. brucei* have spread beyond the "tsetse fly belts" where transmission is principally by *Tabanus* spp.
ERADICATION AND CONTROL

**Vector control:** Fly eradication is the only effective trypanosomiasis control method now available. Several approaches to fly control have been used with varying degrees of success.

Discriminative bush clearing, extensively used in early tsetse fly eradication campaigns, has been locally useful in that it eliminates the breeding places of the tsetse, but to be completely effective it requires ecologically unacceptable destruction of vast areas of bush and forest. It is still a useful procedure when used locally in conjunction with other control methods.

Game elimination, and thus elimination of the main source of blood-meals for the tsetse, was used in early eradication campaigns but it is an ineffective and wasteful procedure with little to recommend it.

Application of the sterile male technique (as used in screwworm eradication in the USA) is receiving considerable attention at this time. Early problems with breeding of the male flies have been overcome and field trials are underway in both East and West Africa to determine the effectiveness of this approach to vector control. The very slow breeding characteristics of the tsetse flies and the resultant problem of breeding sufficient male flies for an effective campaign at acceptable cost, may make the sterile male technique economically unfeasible.
Attempts to use tsetse fly parasites and predators have not been fruitful, but since the tsetse flies are susceptible to a considerable number of parasites and predators, this approach to vector control needs to be further explored.

Insecticides, especially organochlorine products have been extensively used in tsetse fly eradication schemes. The most commonly used insecticides are DDT and dieldrin, the former being the product used to eradicate the tsetse fly from Zululand in South Africa. Eradication of the fly from other parts of Africa would be feasible only if considerable international cooperation can be accomplished. Insecticide eradication, while feasible, has the tremendous disadvantage of also eradicating many other arthropods, many of them desirable species.

Chemotherapy and Chemoprophylaxis:

The use of drugs for the treatment and control of nagana has been important for many decades, but the rapidity with which the trypanosomes have developed resistance to each drug introduced has tremendously complicated this approach to nagana control. Some of the older chemoprophylactic drugs such as the quinapyramine derivatives "Antrycide" and "Antrycide Prosalt" are still widely used and give effective protection against T. b. brucei infection in horses, camels and cattle for up to three months. The drug pyrithidium bromide ("Prothidium" and "AD2801") are useful in the prophylaxis of T. vivax and T. congoense infections in cattle, sheep and goats, and can give protection for up to six months. The most widely used of the newer drugs, and also the least expensive,
are the isometamidium chloride drugs "Samorin", "Trypanmidium" and "M&B 4180A", which are excellent for the prophylaxis of all three nagana trypanosomes, giving protection of up to six months. When trypanosome resistance to a drug develops it is common practice to switch to another unrelated compound, or to use two drugs simultaneously.

A very widely used chemotherapeutic drug is diminazine aceturate ("Berenil") which is effective against all three nagana trypanosomes. The isometamidium drugs are also excellent chemotherapeutic drugs as are the quarternary ammonium trypanocides "Antrycide", "Ethidium" and "Prothidium".

While extensively used in nagana control, chemoprophylaxis is an expensive, time-consuming and thus unsatisfactory solution to the problem of nagana.

**Immunization:**

There is currently no vaccine available for nagana. Attempts have been made to immunize animals against nagana by infection and treatment, but these attempts have not been successful. It is clear that an effective vaccine would be of inestimable value, and thus research aimed at the development of a vaccine continues. The major constraint to the development of an effective vaccine has been the remarkable ability of the trypanosomes to undergo antigenic change. It is clear that an effective vaccine would need to contain a wide spectrum of the surface antigens referred to as variable antigen types (VATs), a seemingly impossible task since the purification and analysis of these VATs has not in the past been possible. The recent development of methods for the in vitro cultivation of trypanosomes however, is allowing sophisticated antigenic analysis, and the
prospects for the development of effective vaccines are now much brighter.

**Immunotolerance:** It has long been recognized that certain breeds of cattle are considerably more resistant to nagana than other\textsuperscript{6,10,46}. This is especially true of the so-called West African short-horned cattle\textsuperscript{50} (also known as the Muturu, Baoule, Laguna, Samba or Dahomey cattle\textsuperscript{17}) and the N'dama breed\textsuperscript{6,46}, also of West Africa. Susceptibility studies\textsuperscript{46} have shown the N'dama to be the most resistant breed, followed by the smaller West African short-horned cattle, with the large Zebu being the most susceptible.

The mechanisms of trypanotolerance have been extensively studied\textsuperscript{43} and it is now well established that trypanotolerance has a genetic basis. It appears that the resistant N'dama and the susceptible Zebu differ mainly in the quality of the immune response launched by the host in response to infection, the N'dama being intrinsically more capable of resisting infection. Since the N'dama are a small breed and the Zebu a large, more desirable breed, crossbreeding experiments have been carried out in an effort to produce a large resistant breed. Unfortunately the result has been a product of intermediate size and intermediate susceptibility to trypanosomiasis\textsuperscript{17}. It has been shown, however, that the very resistant N'dama cattle, while considerably smaller, are as productive as the Zebu on a feed conversion basis\textsuperscript{43}.

Trypanotolerance in sheep and goats has also been described, but the mechanisms of the tolerance phenomenon have not been defined\textsuperscript{43}.

**Future for control of the disease:** Due to relaxation of fly control methods and chemoprophylaxis campaigns the impact of nagana is actually increasing in many parts of Africa. Little will be done to control this disease until a concerted international campaign is launched against the tsetse flies.
Unfortunately adequate methods for a successful continent-wide campaign are not yet in hand. The recent establishment of the International Laboratory for Research on Animal Diseases (ILRAD) in Kenya, with its emphasis on the development of better understanding of the antigenicity of the trypanosomes and the immunological responses of their hosts, could be a major step toward the development of an effective vaccine against nagana. Until such a vaccine emerges, or unless a truly excellent chemoprophylactic drug is found, nagana will remain the most important livestock disease of Africa, and will continue to bring misery to untold millions of Africa's inhabitants.
SOCIO-ECONOMIC ASPECTS

It is evident from the many published reports that African Animal Trypanosomiasis presents a major obstacle to the development of equatorial Africa by limiting food production, economic gain, and by causing disease and death in man. It is estimated that some 35 million people and approximately 25 million cattle are exposed to the risk of infection; in vast areas of the African continent, breeding of domestic stock is impossible due to the high incidence of the disease. Livestock populations at risk to the disease are shown in Table 1.

The significance of the tsetse transmitted trypanosomiasis problem comes from the necessity of most African governments to provide an adequate food supply for a rapidly increasing human population which is requiring a better quality of diet. Most governments are therefore seeking to increase overall food production and also to increase the availability of protein which in many densely populated areas is notably deficient.

This fact was underscored during the World Food Conference which met in Rome, November 5-16, 1974. A resolution was passed at this conference which declared:

Recognizing the importance of African animal trypanosomiasis as a major limiting factor to rural development in general and animal production in particular in a large number of African countries,

Taking note that progress in trypanosomiasis and tsetse control techniques now makes possible the implementation of large-scale operations,
Table 1. Livestock Populations of Selected African Countries (1975)

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<thead>
<tr>
<th>Country</th>
<th>Livestock population¹/</th>
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<tbody>
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¹/ From the FAO/WHO/OIE Animal Health Yearbook, 1975, FAO, Rome.
Table 1 (Cont.) Livestock Populations of Selected African Countries (1975).

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<tr>
<th>Country</th>
<th>Bovines</th>
<th>Small ruminants</th>
<th>Swine</th>
<th>Equines</th>
<th>Camels</th>
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<td>41 330 000</td>
<td>1 541 000</td>
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<tr>
<td>Sudan</td>
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<td>23 000</td>
<td>161 000</td>
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<td>Toto</td>
<td>220 000</td>
<td>1 388 000</td>
<td>237 000</td>
<td>3 000</td>
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<td>Uganda</td>
<td>4 100 000</td>
<td>2 450 000</td>
<td>75 000</td>
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<td>143 000</td>
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<td>991 000</td>
<td>2 995 000</td>
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Recognizing that the effective implementation of an internationally coordinated programme for the control of African animal trypanosomiasis would open us vast areas of land for animal and crop production thus providing the potential for greatly increased animal protein and other food supplies both to overcome deficits in the African continent and to provide surpluses for export,

Recognizing the socio-economic benefits which would accrue to rural populations from such a programme, including a significant contribution to the control of human trypanosomiasis,

Taking note that trypanosomiasis and tsetse control should be considered as the first phase of an integrated plan of economic development to be followed by projects covering appropriate land and water conservation and utilization, including forestry, pasture improvement, livestock management, animal health, livestock marketing and processing, as well as training in their various fields,

1. **Recommends** that FAO in cooperation with the governments of the countries concerned, interested international organizations and specialized research institutes, and with the support of bilateral and multi-lateral assistance agencies, launch as a matter of urgency a long-term programme for the control of African animal trypanosomiasis as a project of high priority;

2. **Calls for** immediate establishment of a small Coordinating Unit at FAO Headquarters to start the first phase of the Programme devoted to training, pilot field control projects and applied research, in preparation for future large-scale operations;
3. **Recommends** that FAO take immediately the necessary steps to mobilize the funds and services required for the Programme.

The Food and Agriculture of the United Nations responded to these recommendations made by the World Food Conference with the development of a "Programme for the Control of African Animal Trypanosomiasis". In their program, the FAO described both direct and indirect consequences of the disease, African Animal Trypanosomiasis as follows:

**The direct consequences**, represented by the economic losses due to the disease and to various expenditures incurred in controlling it. They comprise:

(a) mortality;
(b) disease, which manifests itself in emaciation, retarded growth, abortion, temporary sterility and various organic lesions;
(c) the cost of detection and treatment of infected animals (veterinary service personnel, trypanocidal drugs, equipment, operating expenses);
(d) the cost of preventive operations (chemoprophylaxis, tsetse fly control, development of trypanotolerant livestock;
(e) the cost of research on animal trypanosomiasis control.

**The direct consequences** of animal trypanosomiasis affect:

(a) **human health**, as the shortage of meat and milk causes protein deficiencies which are particularly harmful to children;
(b) **agriculture**, because the lack of draught animals and manure reduces agricultural output;
(c) **livestock production**:
   (i) trypanosomiasis limits the possibilities of introducing improved breeds, which are highly sensitive to this disease, thus preventing the upgrading of local livestock by crossing with
   (ii) the presence of trypanosomiasis causes livestock to be concentrated in safe grazing areas, which results in their overuse and deterioration;
(iii) Seasonal variations in the incidence of trypanosomiasis prevent some pastures from being grazed throughout the year and compel herdsmen to practice transhumance, which holds them back from integration in the national community;

(d) **the economy**: the deficit in animal production compels countries where trypanosomiasis is rife to resort to imports of meat and dairy products, a practice harmful to their balance of trade.

An additional, indirect consequence not listed by the FAO is that of disease in humans. Wild and domestic animals serve as the main reservoirs of *Trypanosoma brucei rhodesiense* which causes an acute type of trypanosomiasis in humans. This public health hazard results in human deaths and sicknesses which in turn reflects in under-utilization of land and in the loss of work force.

As justification for their proposed control program the FAO stated:

To evaluate the profitability of the Programme, one can try to estimate the meat production of the regions concerned, if the disease were controlled, on the basis of the following criteria:

- area of the tsetse-infected zone which could be used for livestock raising: 7 million Km$^2$;
- average potential density: 20 cattle per Km$^2$;
- total potential population of infected zone: 140 million head;
- present population: 20 million cattle;
- possibility of increasing the cattle population: 120 million head;
- average productivity in Africa: 12.5 kg per head per year;
- additional meat production: 1.5 million tons per year;
- value of additional meat production (basis of 50 cents per kg): U.S. $750 million.

There are many other publications in which the socio-economic impact of African Animal Trypanosomiasis is discussed. Among them are two major reports, "The African Trypanosomiasis" by a joint WHO Expert Committee and FAO Expert consultation on the African Trypanosomiases, and "Tsetse and Trypanosomiasis Control - A Strategy for the Future" made by an
international task force under the auspices of the Inter-African Bureau of Animal Resources.

In their report, the WHO and FAO Expert Committees stated:

The trypanosomiases in Africa are still the most serious threats to the health of man and a serious obstacle to the development of agriculture industry. It is estimated that some 35 million people and approximately 25 million cattle are exposed to the risk of infection. In vast areas of the continent breeding of domestic stock is impossible due to the high incidence of the disease.

The report made by the task force under the auspices of the Inter-African Bureau of Animal Resources describes the economic impact of African Animal Trypanosomiasis as follows:

Throughout the 36 countries in tropical Africa in which it prevails, trypanosomiasis causes more losses of livestock than does any other disease. It kills or disables camels, horses, pigs, sheep, and goats. The incidence of the disease ranges within wide limits according to the tsetse species prevalent, the density of infestation, the species of trypanosomes carried, the rate of infection, and the feeding preferences of the flies, to mention but a few of the factors. Much of the forest and savanna zones constitute high-risk areas, and in such areas trypanosomiasis prohibits exploitation of abundant fodder resources.

Two sub Species of Trypanosoma brucei cause sleeping sickness in human beings. T. b. rhodesiense, which is spread roughly from Ethiopia to Botswana, produces an acute or subacute form of the disease. T. b. gambiense typically causes a chronic form from the eastern shores of the Rift Valley Lakes westward to the Atlantic coast, from Angola in the south, to Senegal in the north.
REFERENCES


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It has been shown that a great body of knowledge concerning African Animal Trypanosomiasis exists as evidenced by the large number of citations given in this study. Major advances, which have served to fill in many previous information gaps, have occurred in the last ten years. Yet, the necessary information to develop satisfactory control methods for African Animal Trypanosomiasis is still inadequate. As an example, a vaccine against trypanosomiasis is badly needed, yet it is still only a research objective.

It was evident from personal discussions with experts in the field and from the many published reports that African Animal Trypanosomiasis is the most serious obstacle limiting the development of equatorial Africa. It limits food production, economic gain, and causes disease and death in man. It is estimated that some 35 million people and approximately 25 million cattle are exposed to the risk of this disease. In vast areas of the African continent the breeding of domestic stock is impossible due to the high incidence of the disease. It has been estimated that the tsetse fly infests approximately five million square miles of Africa. Approximately three million square miles of this area is covered by a thick forest.

Several major studies have been made within the last few years on the need for African Animal Trypanosomiasis research. Parts of the reports from two of these studies are given in this section.

In the 1979 "Report of a Joint WHO Expert Committee and FAO Expert Consultation" several task force recommendations were given as to priorities in research on African Trypanosomiasis. A discussion of these priorities is given below:
The various areas of trypanosomiases research are closely interrelated in techniques and planning. The Special Programme for Research and Training in Tropical Diseases launched by WHO and of the long-term programme for the control of animal trypanosomiases in Africa anticipated by FAO considered it necessary to identify the areas of research for current control needs. Therefore, among the research needs dealt with in detail in Section 11, the Committee recommended the following order of priority.

**Training** - The first priority for FAO and WHO should be to promote the establishment of a national core of experts in trypanosomiases control and of research specialists.

1. **Drug development** - For both human and animal trypanosomiases, the second priority should be the development of trypanocides. Here, the fundamental approach and the systematic screening of new compounds are of equal importance.

2. **Epidemiology and epizootiology, and current control methods** - For the human disease, emphasis should be laid on developing: methods of identification of pathogenic *Trypanosoma*, which are also crucial for animal reservoir studies; easily applicable tools for detecting infection in man; and simple means for reducing man-fly contact at the community level. For the animal disease, the economic evaluation of the trypanosomiases in livestock and on cost-benefit analyses of trypanosomiases control in various circumstances should be emphasized, comparing different methods or various combined approaches.

3. **Pathogenesis** - For WHO, the next priority should be research on the pathogenesis of the disease, with particular reference to adverse side effects during treatment and to the immunopathological aspects. The main approaches required are experimental pathology and biopsy-autopsy studies in man.

These are the major areas relevant to the WHO Special Programme for Research and Training in Tropical diseases. The six other areas considered of particular importance were:
(4) **Vector control by chemical methods** - It is recommended that FAO studies be carried out to improve methods for large-scale operations by aerial application, particularly in the dry savanna zone. In the Human trypanosomiases field, WHO should promote studies to improve techniques of aerial application of insecticides in the moist savanna as well as investigations on simple vector control systems suitable for self-help schemes by the rural population.

(5) **Antigenic variation and immune protection** - An understanding of the mechanism of antigenic variation may lead to a new insight into the immune pathology and create new possibilities for chemotherapy. This seems an essential step in the search for a vaccine, which would be very helpful in the control of trypanosomiases in domestic animals.

(6) **Trypanotolerance** - A study of the mechanisms responsible for this phenomenon found in cattle trypanosomiases could help clarify the phenomenon of symptomless carriers in man.

(7) **Systematic treatment of cattle** - This type of treatment, together with the controlled use of chemotherapeutics including prophylactic drugs as a means of trypanosomiases control, should be further investigated and standardized.

(8) **Vector control by biological methods** - For both animal and human trypanosomiases, biological control of tsetse needs much investigation. It could open up entirely new aspects in the control strategy.

(9) **Land use** - Criteria for comprehensive planning in land use should be defined and their application encouraged not only by FAO but also by WHO.

Another report "Tsetse and Trypanosomiasis Control - A Strategy for the Future" was made in 1979. Recommendations for research contained in this report are:

1. The Task Force **recommends** intensifying studies on biology, ecology, behavior, and vectoral capacity of tsetse. New discoveries on these subjects may contribute to better uses of insecticides and other methods of tsetse control more effective than those presently in vogue.
2. The Task Force recommends that:
(a) Investigations continue on the search for selective uses of existing insecticides to reduce the hazard of any long-term adverse effects on these chemicals on the environment;
(b) Research and development be conducted with a view toward adopting new insecticides more effective and less persistent than those now in use;
(c) Applied research be encouraged to assess the suitability of aerial applications used for treating various types of habitats; and
(d) Equipment for ground-spraying operations be evaluated for its suitability under varying conditions of use.

3. The Task Force recommends that:
(a) The two recently completed major programs of research and pilot studies on SIRM, one in Upper Volta and the other in Tanzania, be thoroughly evaluated as soon as possible for guidance on the potential contributions SIRM may make to integrated control programs for flies; and
(b) Research be accelerated on other methods of controlling the fly, by biological or physiological means, by hybridization techniques, and by actually manipulating the genes of the fly. Should a satisfactory method be developed, Glossina would be particularly vulnerable to this type of control in view of its low reproductive potential.

4. The Task Force recommends that African governments and donor agencies increase their support for research on immunological processes that may lead to the development of anti-trypanosomiasis field vaccines.
5. The Task Force recommends that:
   (a) The productivity of trypanotolerant livestock be studied under different management systems, in different ecological zones, and under varying degrees of trypanosomiasis risk;
   (b) The methodology required for measuring the level of trypanosomiasis risk to which the host is exposed be ascertained; and
   (c) The mechanism, genetics, and environmental determinations of trypanotolerance be researched.

Other documentation which supports the conclusions of this report may be found by reading the abstracts of published literature and current research and by retrieving the literature cited in this report.

Therefore it is recommended that:
(A) The USAID initiate a new five-year program of research on African Animal Trypanosomiasis. This program should be funded with $18,850,000 and should be in addition to present research programs on African Animal Trypanosomiasis funded by the USAID.

This research effort along with present world-wide research efforts should provide new methods of controlling the disease in domestic livestock. It would not be expected to provide the necessary information for eradicating the disease in the very near future.

The five-year program of research advocated in this study should also give the U.S. much more visibility in terms of providing assistance to the developing African nations for coping with this problem. It is believed that this visibility is not adequate at present.

Guidelines on funding were not provided by the USAID and it is impossible to define precise research costs without knowing which countries and institutions would participate in a new research program concerned with African Animal Trypanosomiasis. Therefore, a more definitive estimation of costs will have to await further steps in the development of this program.
It is suggested that this program be composed of projects, of five years' duration, and be conducted in collaboration with a lesser developed country of Africa.

Suggested areas of research are:
1. **Facets of Epidemiology**

   Additional information is needed in several broad facets of epidemiology. These areas of research are (1) to define more precisely the incidence of the disease, (2) to define the kinds and numbers of animals at risk and (3) make a comparison of incidences between areas in which the tsetse has been eliminated for several years with areas in which it has not been eliminated. It is suggested that three projects be supported for a duration of five years.

2. **The Agent**

   The main species of trypanosomes most affecting livestock either individually or associated one with the other are *T. congolense*, *T. vivax*, and *T. brucei*.

   It is evident from a review of the literature contained in this report that these agents have a unique ability to expose various antigenic components to the host. This unique property of the agent poses a major problem in the development of an artificially produced immunity against the agent.

   The nature of research in this area should be concerned with the molecular and cell biology of trypanosomes and with the mechanisms of antigenic variation. Information expected from this research could be used for the development of an immunizing agent.

   Seven projects, to study the phenomenon of antigenic variation and to develop an immunizing agent, should be supported for a duration of five years.

3. **The Vector**

   An elimination of the vector, tsetse fly, represents a fundamental epidemiological approach to controlling the disease. Major advances have been made in the development of methods to control tsetse fly populations. Among those methods are improvements in tsetse fly propagation for use in the sterile insect
release method (SIRM), improved methods of using existing insecticides, the development of new insecticides, methods to capture the tsetse fly or interfere with its reproduction, and methods to decrease habitats for the tsetse fly.

Much more needs to be done in this area. It is recommended that research be supported to study (1) the reproduction system of the tsetse fly, (2) nutrition of the tsetse fly, (3) the ecology and behavior of tsetse manifested after measures for tsetse control have been used and (4) improved methods of tsetse control, such as the SIRM and the selective use of chemicals.

Five projects should be supported for a duration of four years each.

4. The Host and Reservoirs

Recommendations have been made above regarding needed work on the agent which would be directed to the goal of producing artificial immunity. Other facets of host resistance which need additional research are concerned with: (1) chemoprophylaxis, with the prevention of infection, (2) chemotherapy with naturally induced immunological resistance, (3) resistance of wildlife, cattle and sheep, commonly termed trypanotolerance to explain more precisely the scientific basis of this resistance; (4) an extension of the usage of trypanotolerant animals.

Major advances have been made in characterizing different breeds of cattle in Africa on the basis or resistance to trypanosomiasis disease. However, the basis of this resistance is not definitely defined and should be more fully understood.

Chemoprophylaxis or the prevention of disease and chemotherapy with or without resultant resistance to further infection and disease offers much promise and needs further investigation. A search for new drugs to combat African Animal Trypanosomiasis should receive major attention through new research projects.

Six projects concerned with chemoprophylaxis and chemotherapy should be supported for a duration of five years each. Three projects concerned with trypanotolerance should be supported for a duration of five years.

It is further recommended that: the USAID appoint a six-member expert committee to further consider and make recommendations on this important problem of food production, human health and economic development in the lesser developed countries of Africa.